

Supporting Information for

The Role of Tyrosine 71 in Modulating the Flap Conformations of BACE1

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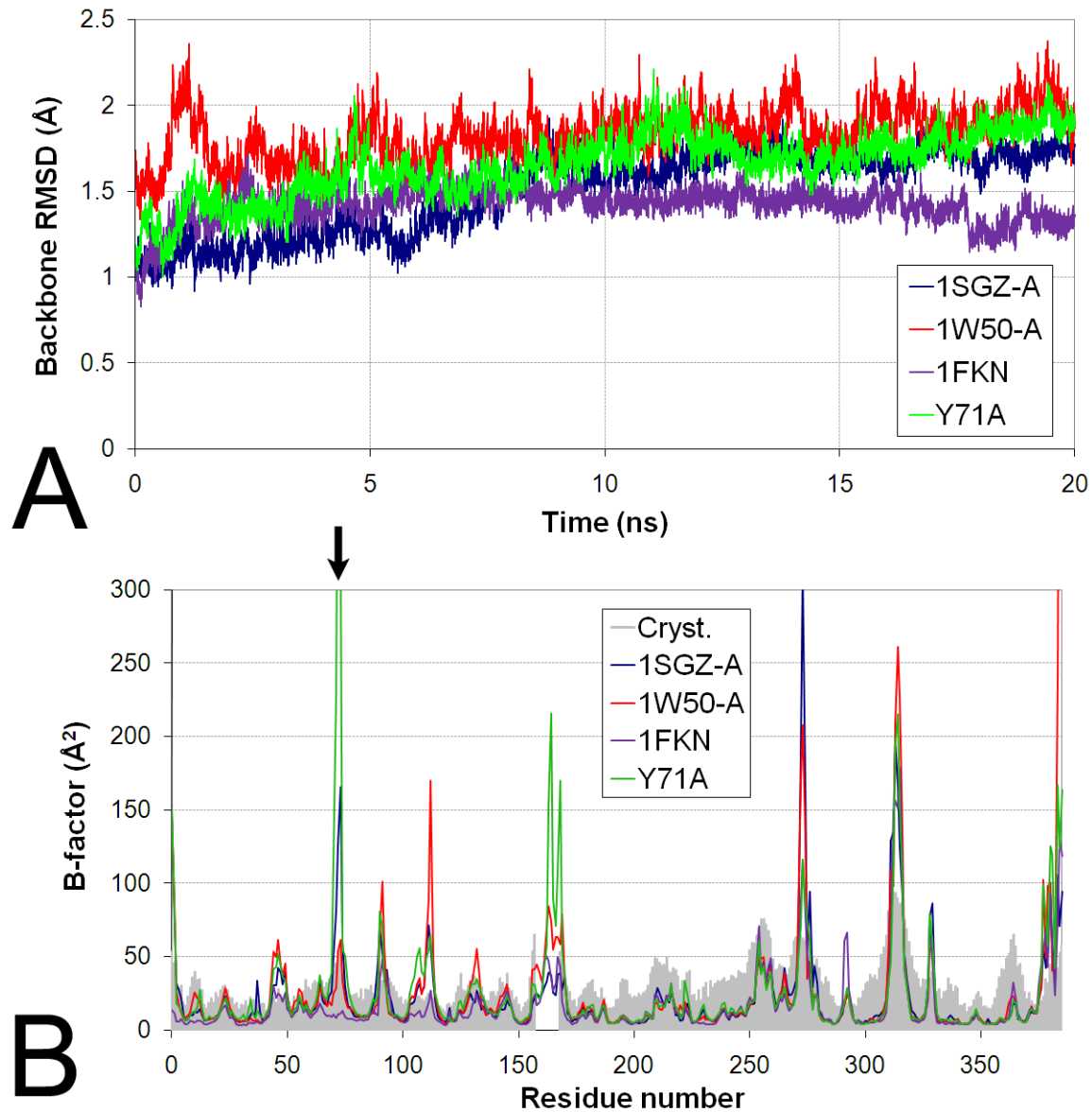


Figure S1. Backbone RMSD values (A) and B-factors (B) calculated from representative simulations initiated from 1SGZ (1SGZ-A), 1W50 (1W50-A), 1FKN, and Y71A. The arrow in B indicates the location of the flap, which has the largest fluctuations in the N-lobe (other than residues 91 and 112 in 1W50-A). The gray lines are the B-factors of the C α atoms in the 1W50 crystal structure.

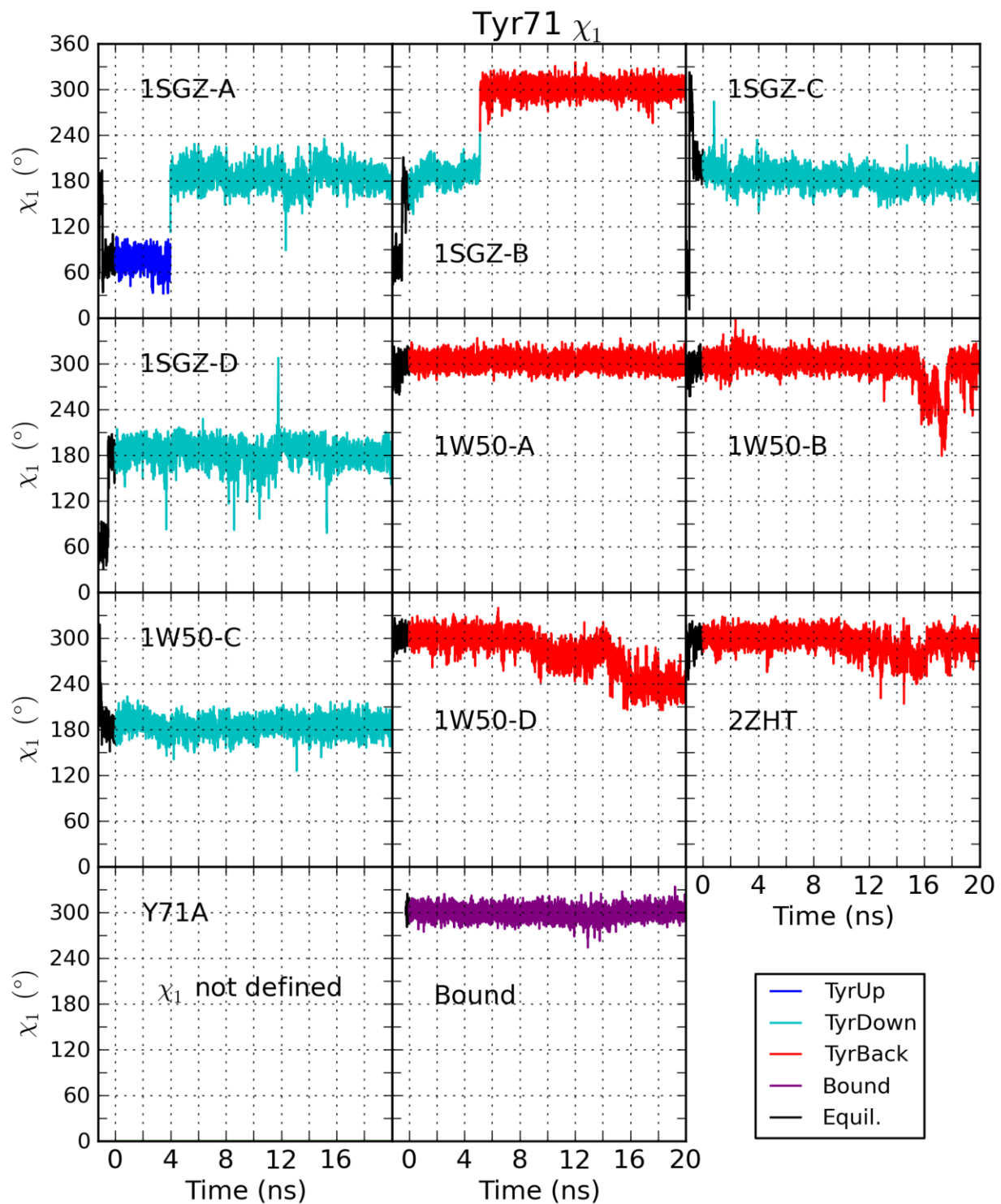


Figure S2. Tyr71 χ_1 values as a function of time for each simulation. The colors indicate the Tyr71 orientation at each time point.

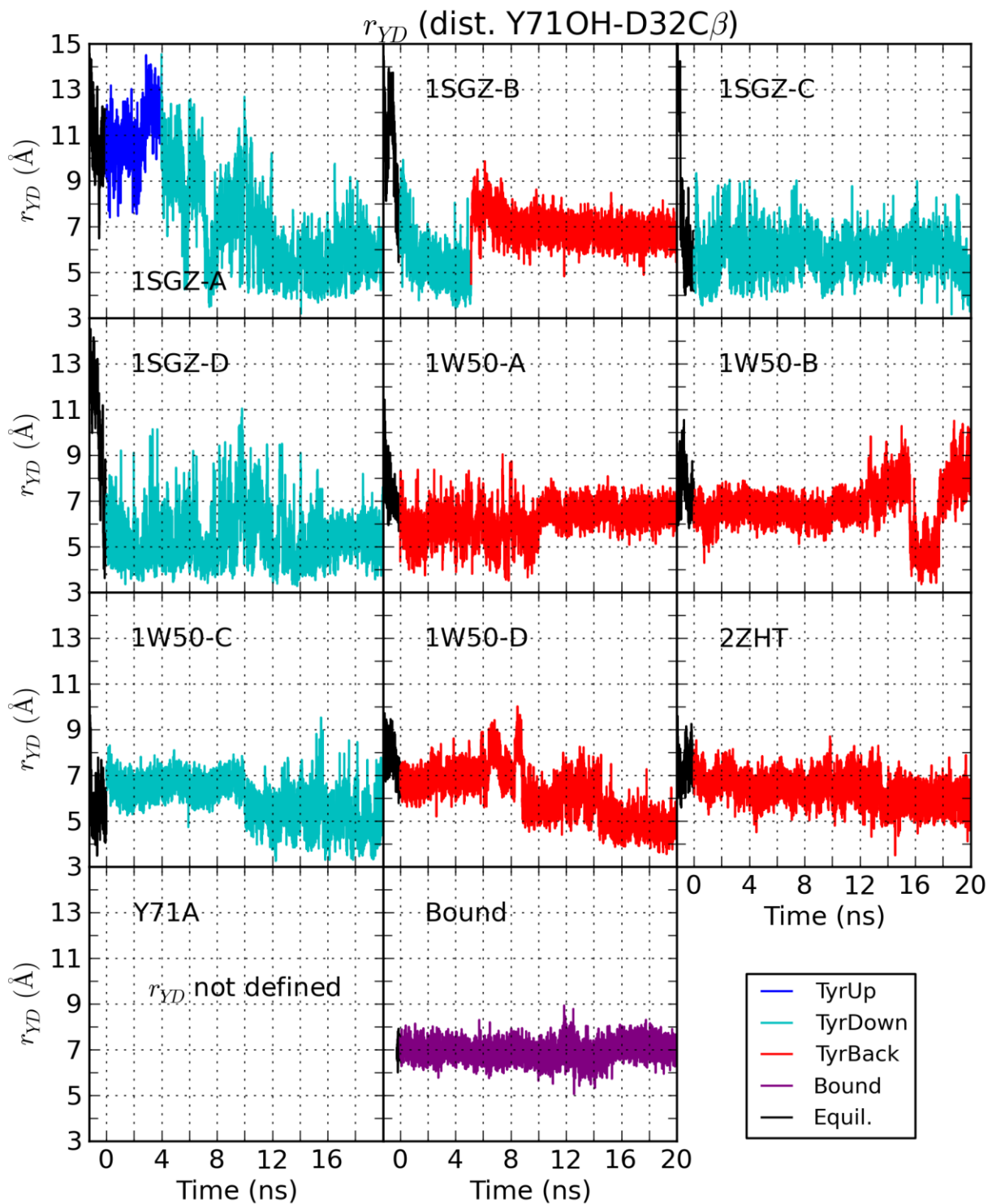


Figure S3. r_{YD} values as a function of time for each simulation. The colors indicate the Tyr71 orientation at each time point.

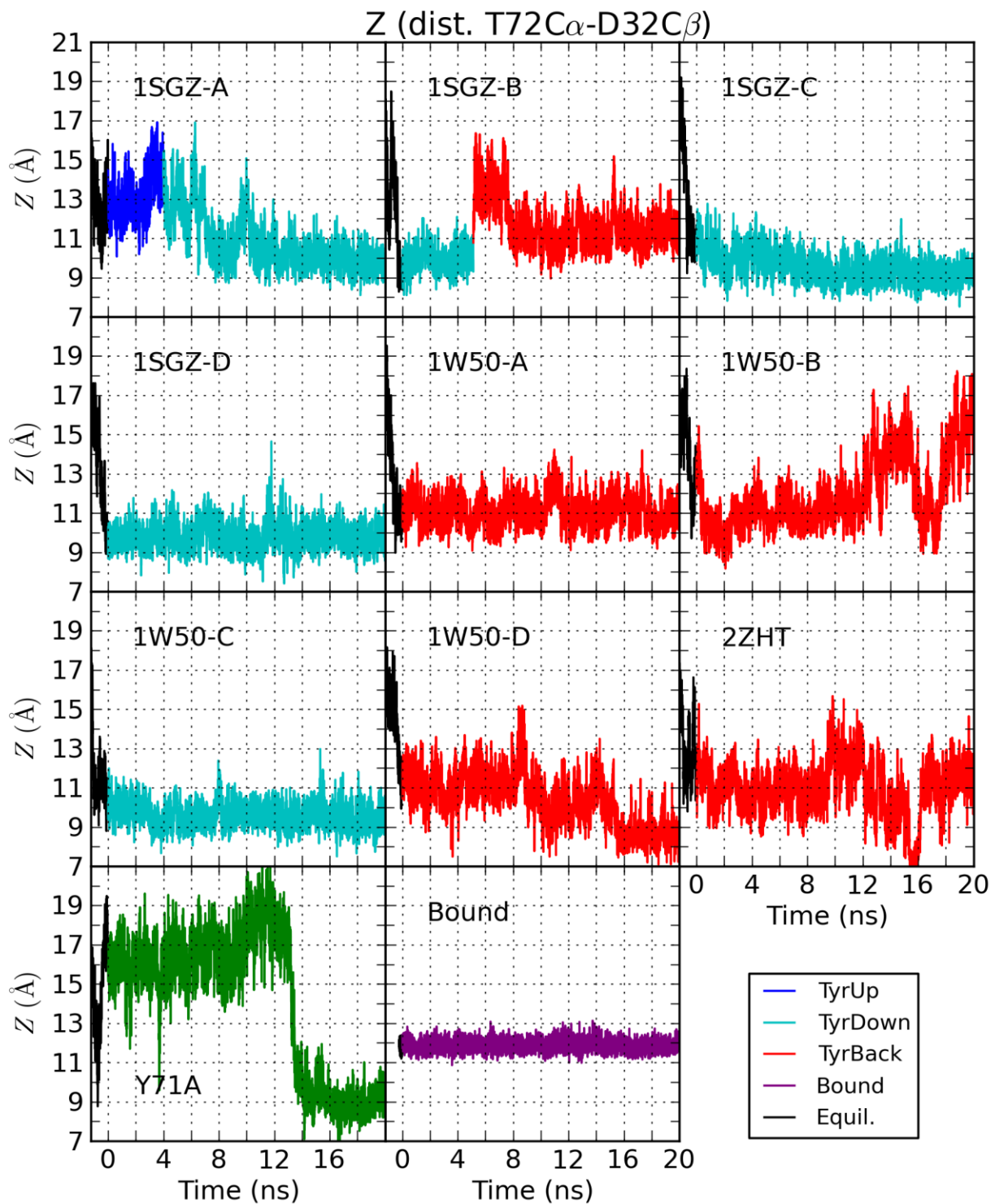


Figure S4. Z values as a function of time for each simulation. The colors indicate the Tyr71 orientation at each time point.

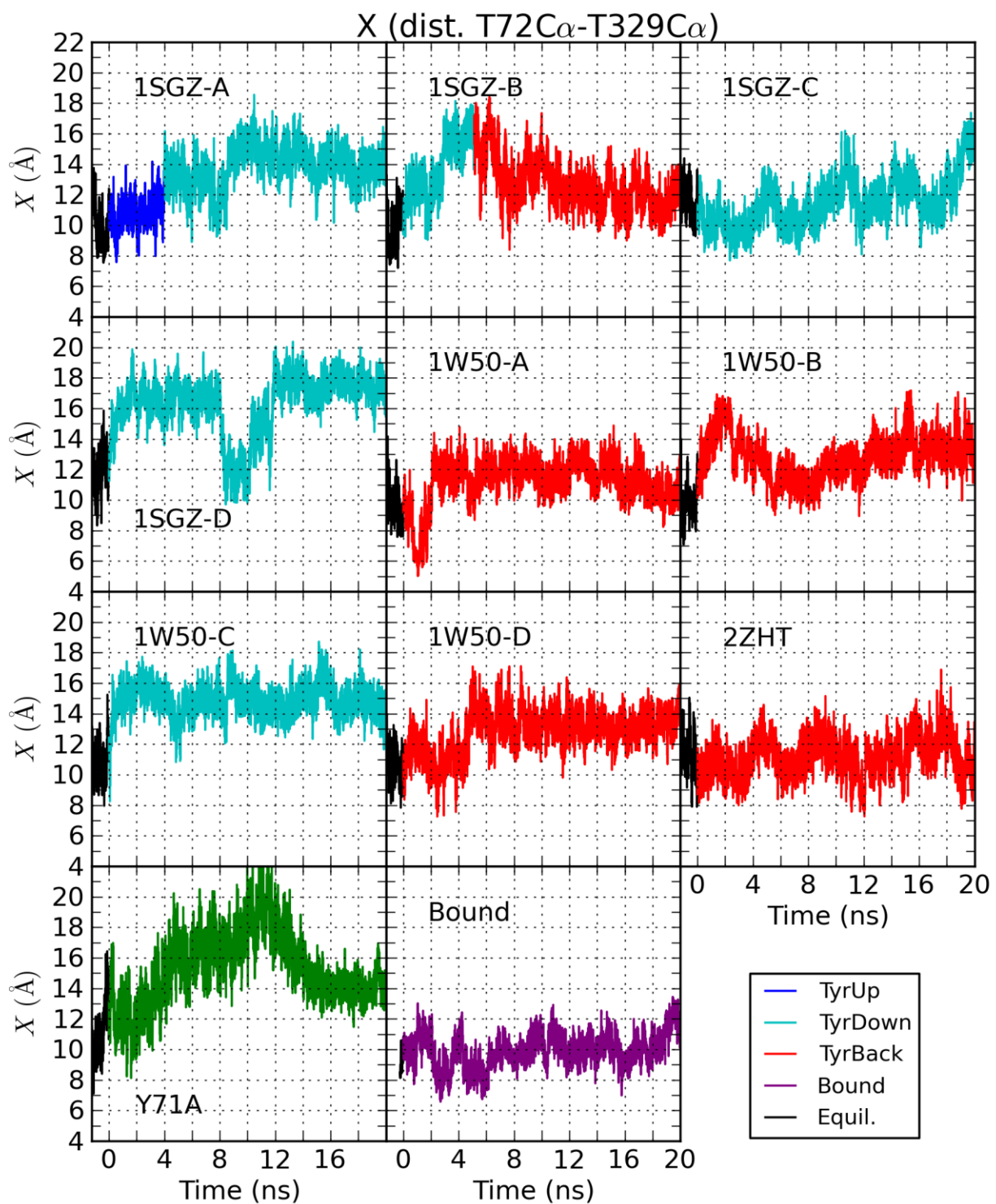


Figure S5. X values as a function of time for each simulation. The colors indicate the Tyr71 orientation at each time point.

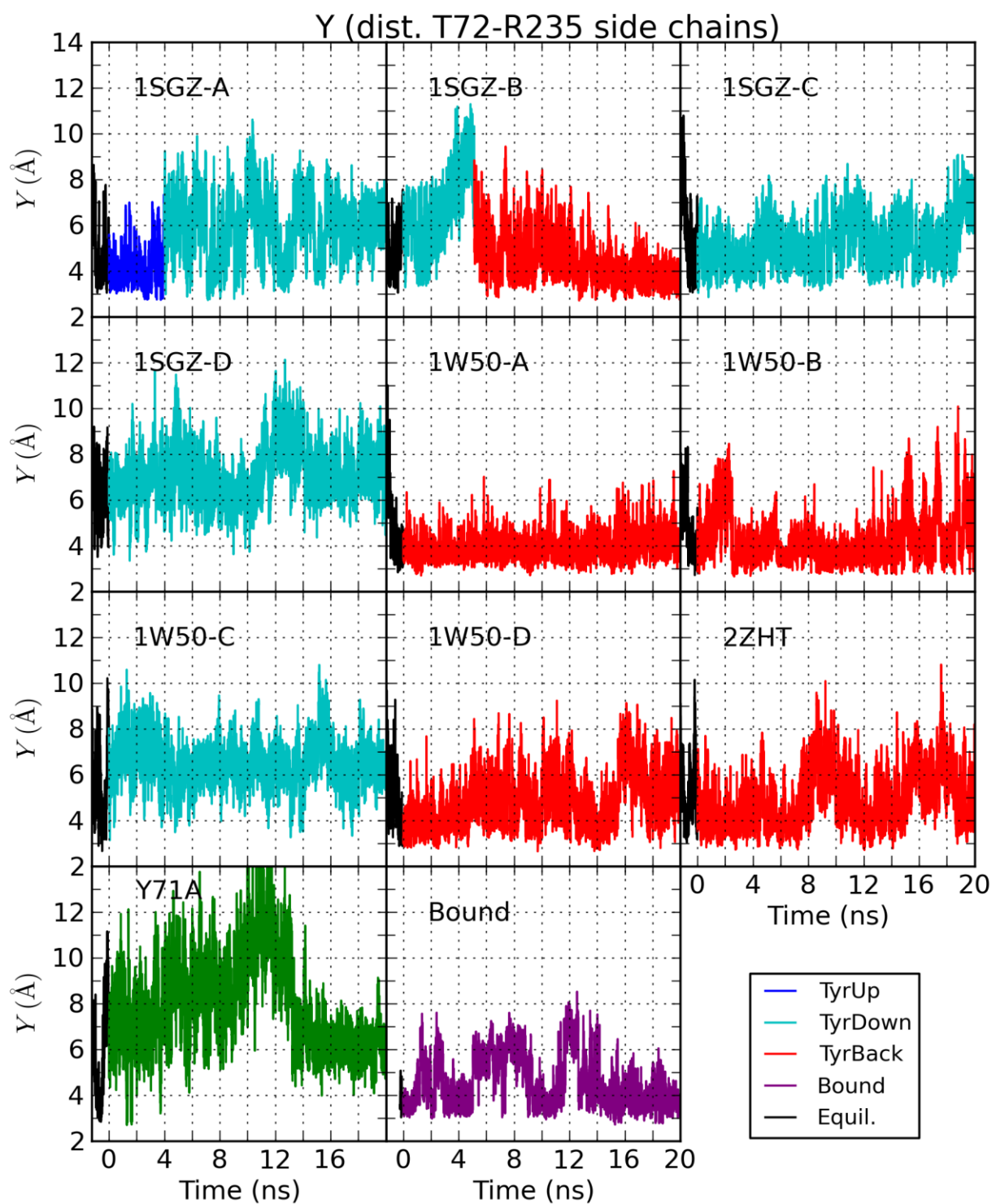


Figure S6. Y values as a function of time for each simulation. The colors indicate the Tyr71 orientation at each time point.

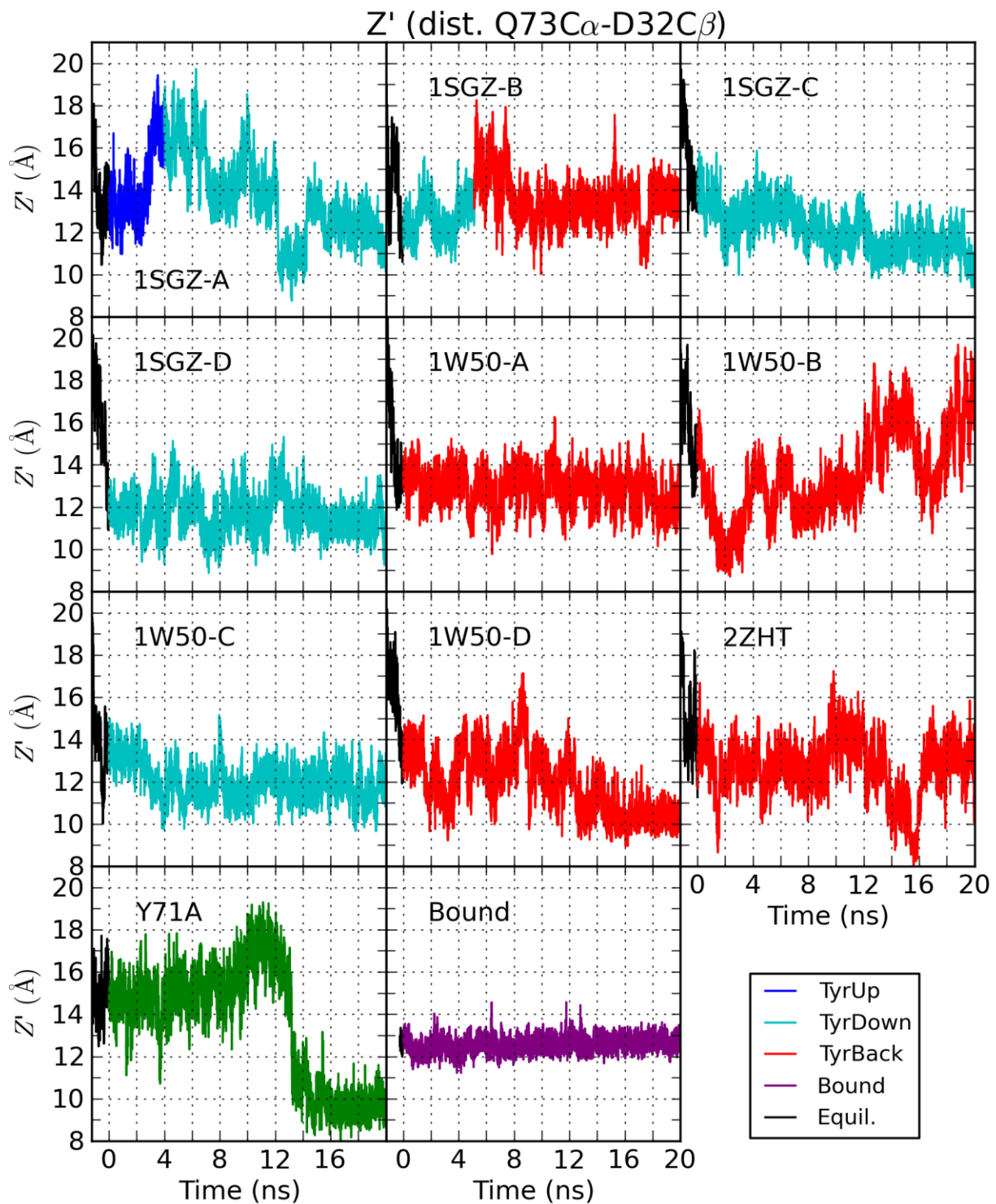


Figure S7. Z' values as a function of time for each simulation. The colors indicate the Tyr71 orientation at each time point.

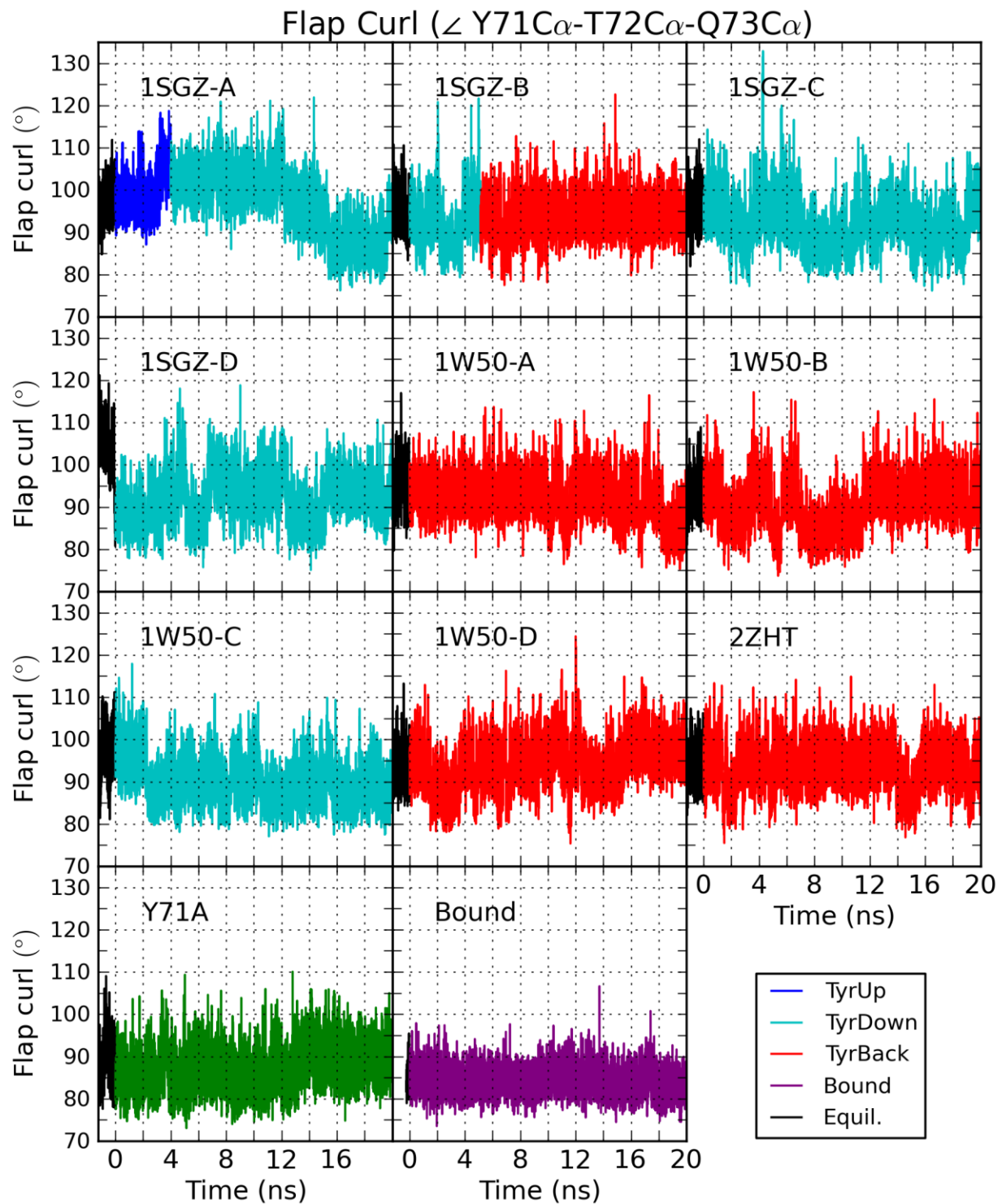


Figure S8. Flap curl values as a function of time for each simulation. The colors indicate the Tyr71 orientation at each time point.

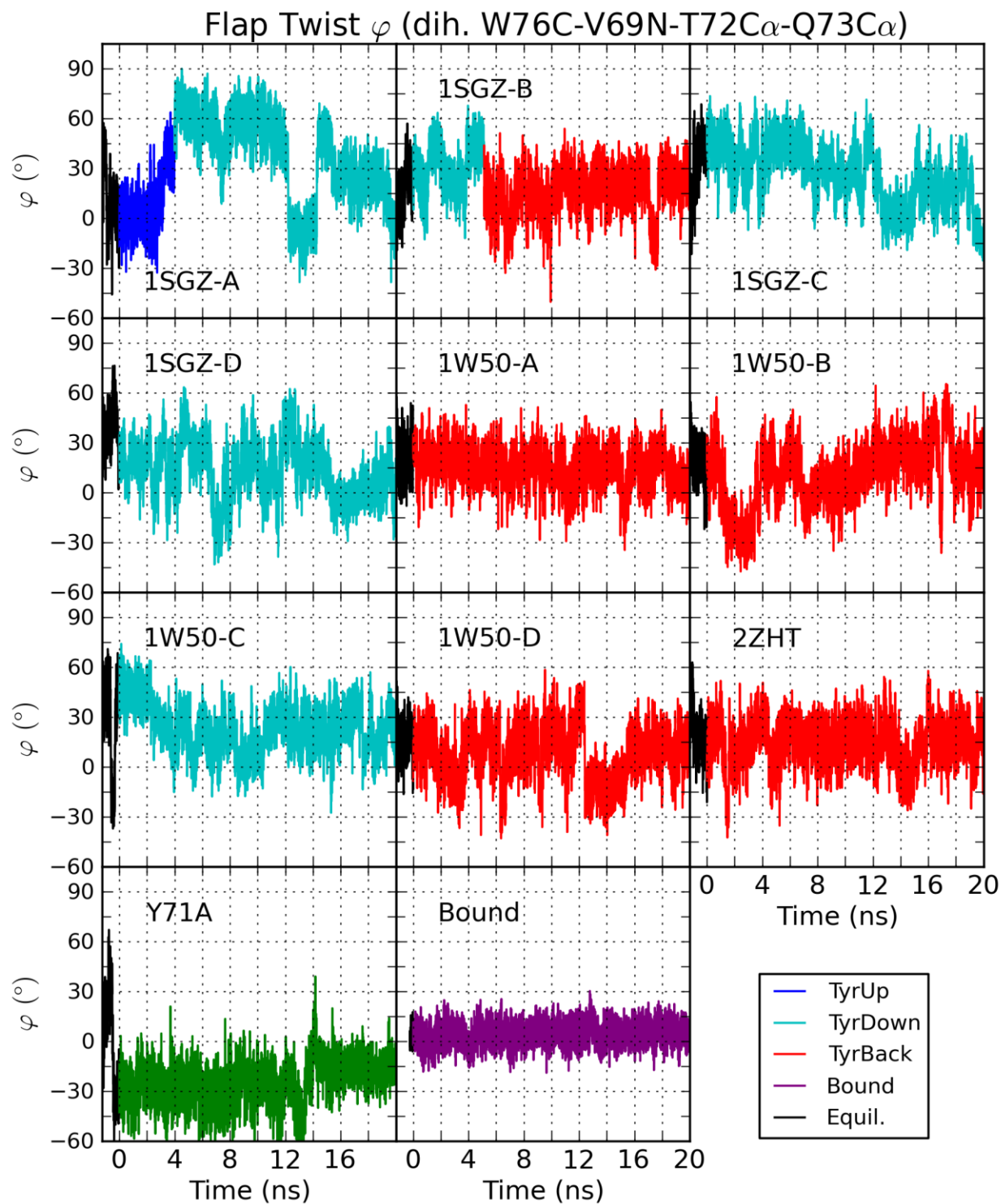


Figure S9. Flap twist φ values as a function of time for each simulation. The colors indicate the Tyr71 orientation at each time point.

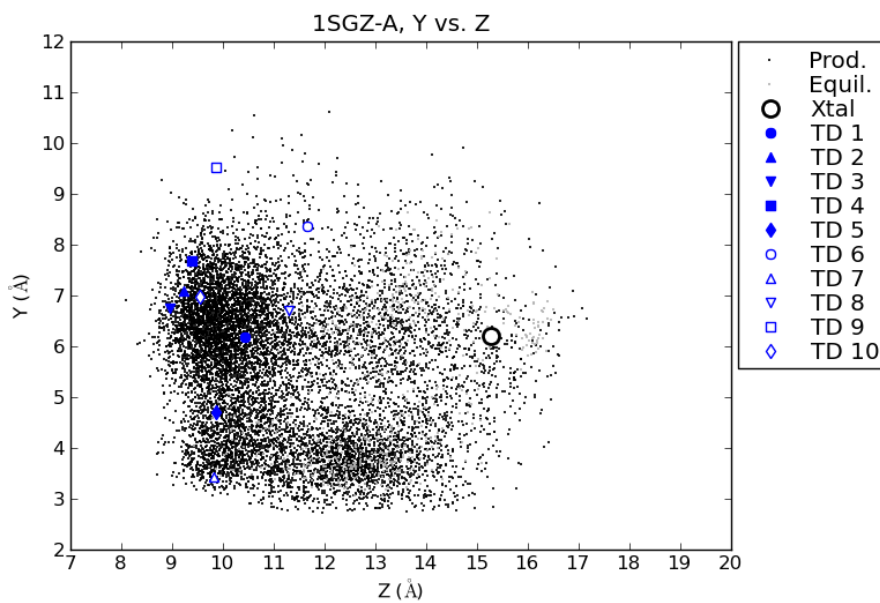
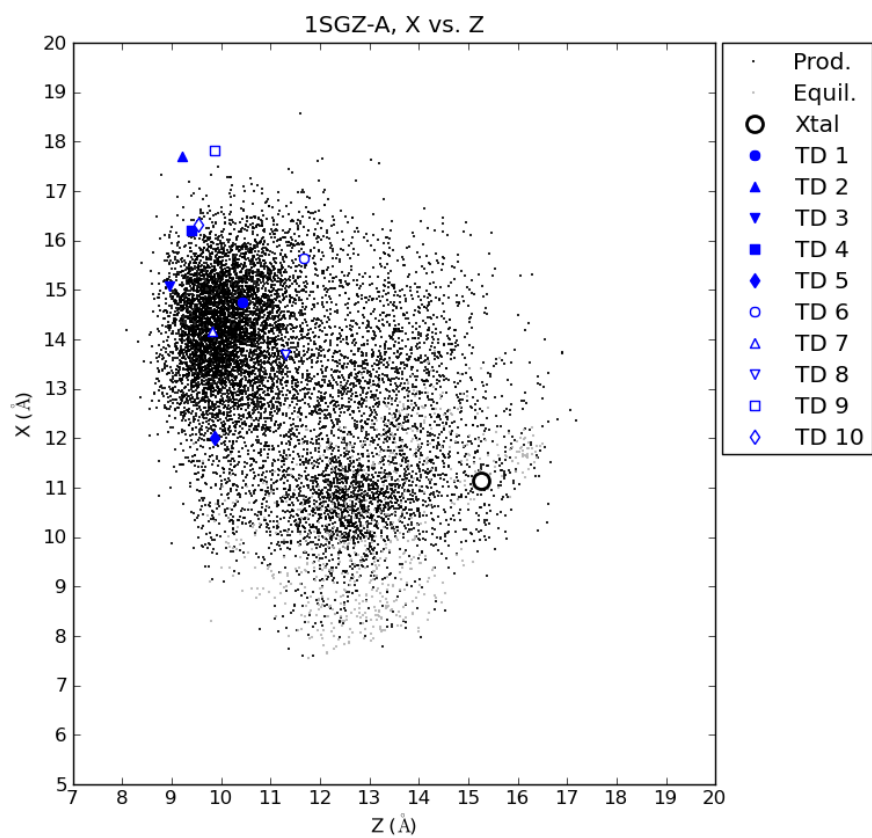


Figure S10. XZ and YZ scatter plots for simulation 1SGZ-A. Relevant centroid values are overlaid (TD: TyrDown centroid).

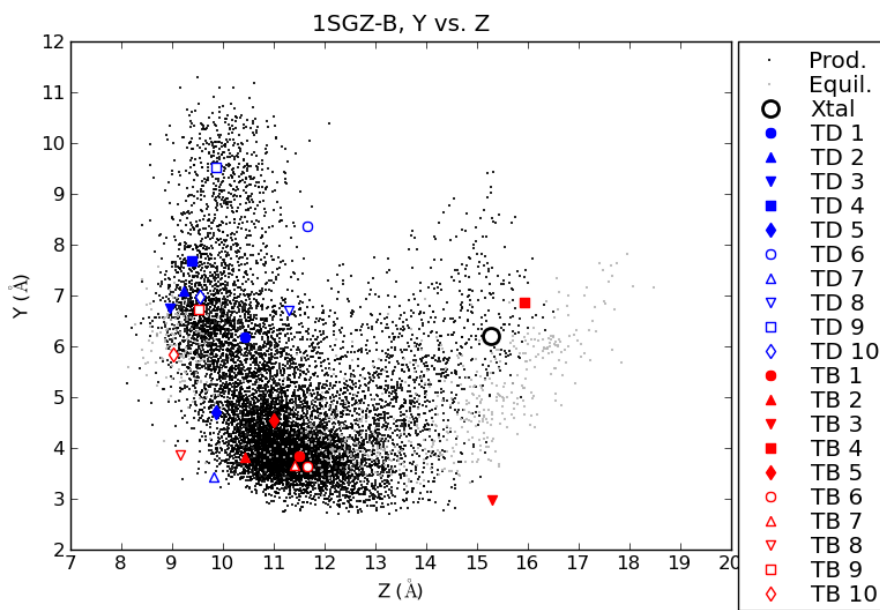
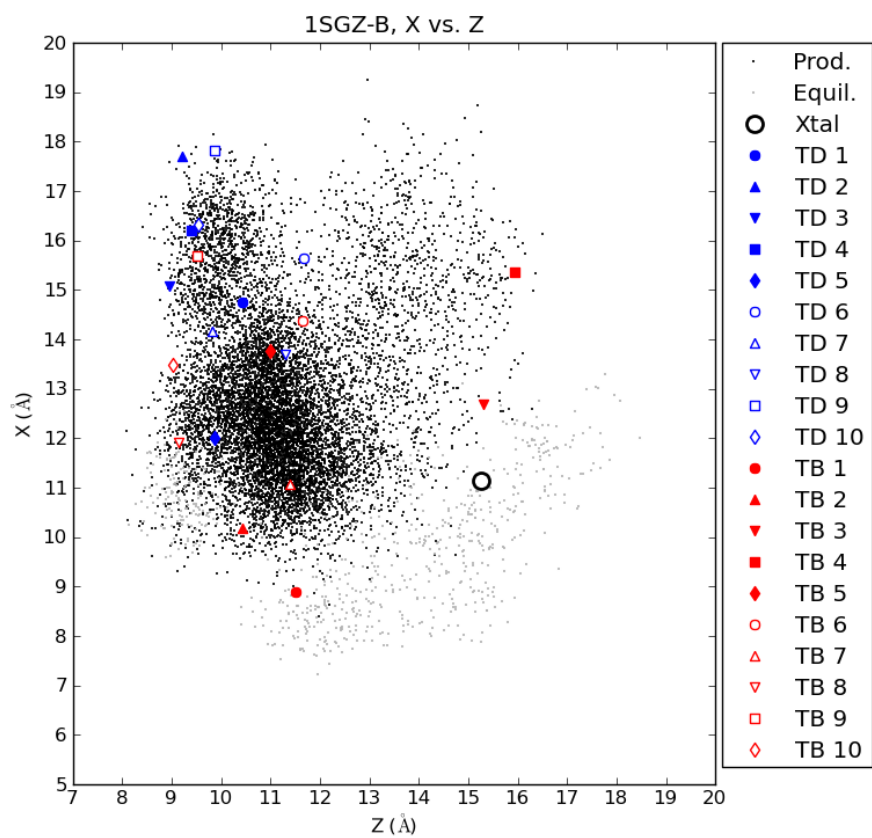


Figure S11. XZ and YZ scatter plots for simulation 1SGZ-B. Relevant centroid values are overlaid (TD: TyrDown centroid, TB: TyrBack centroid).

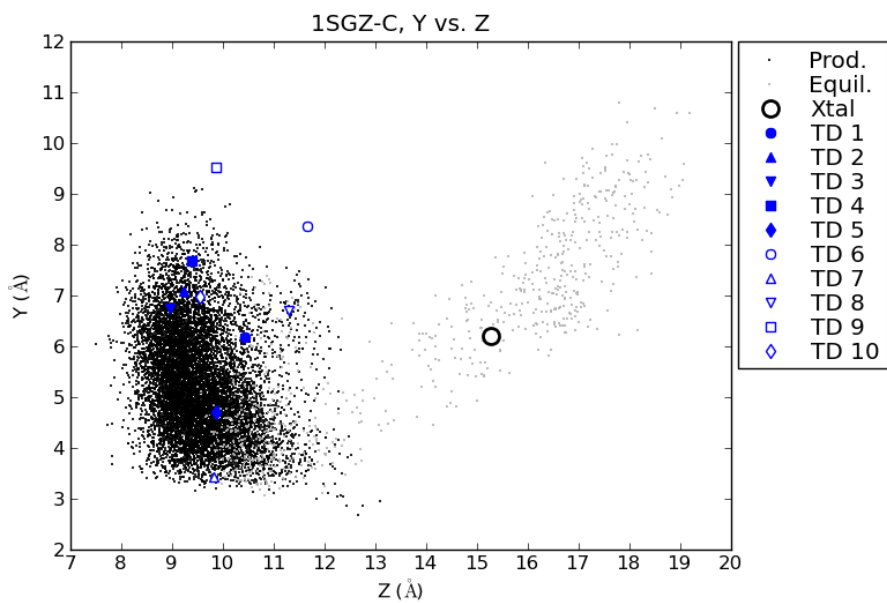
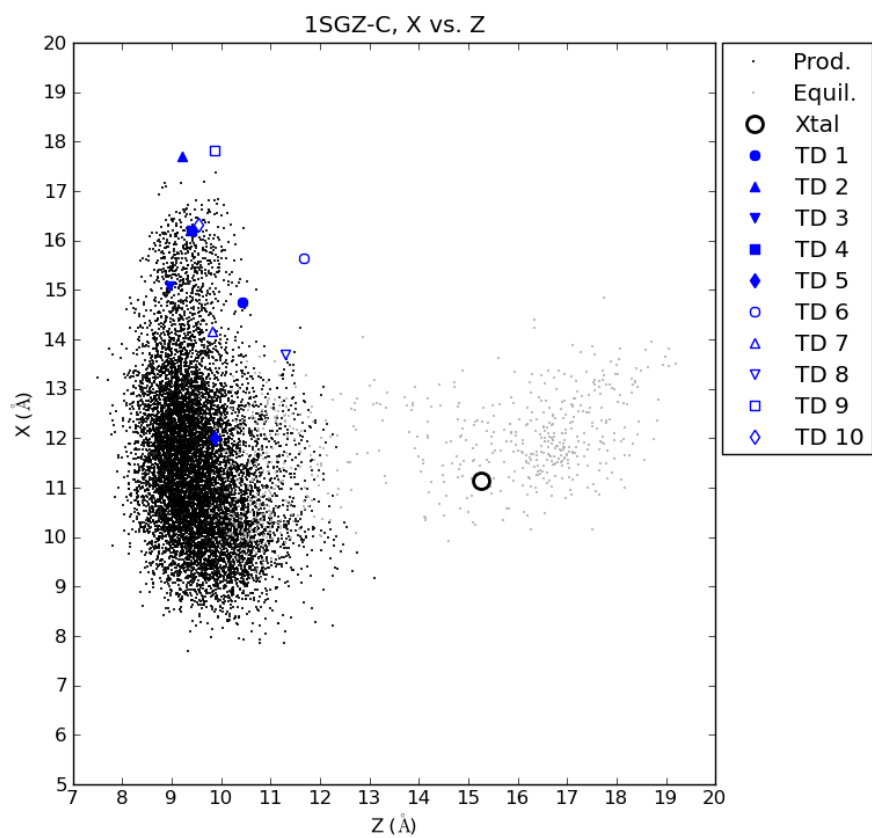


Figure S12. XZ and YZ scatter plots for simulation 1SGZ-C. Relevant centroid values are overlaid (TD: TyrDown centroid).

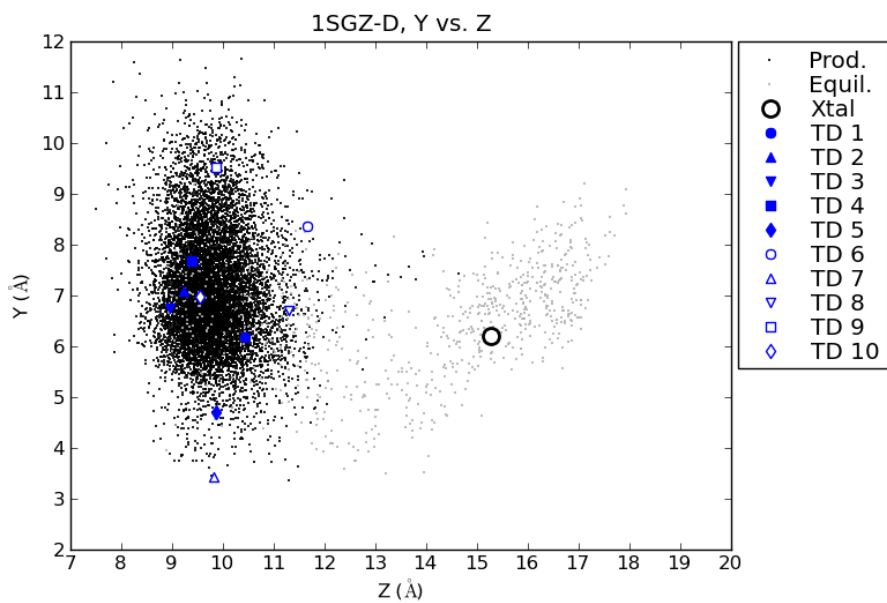
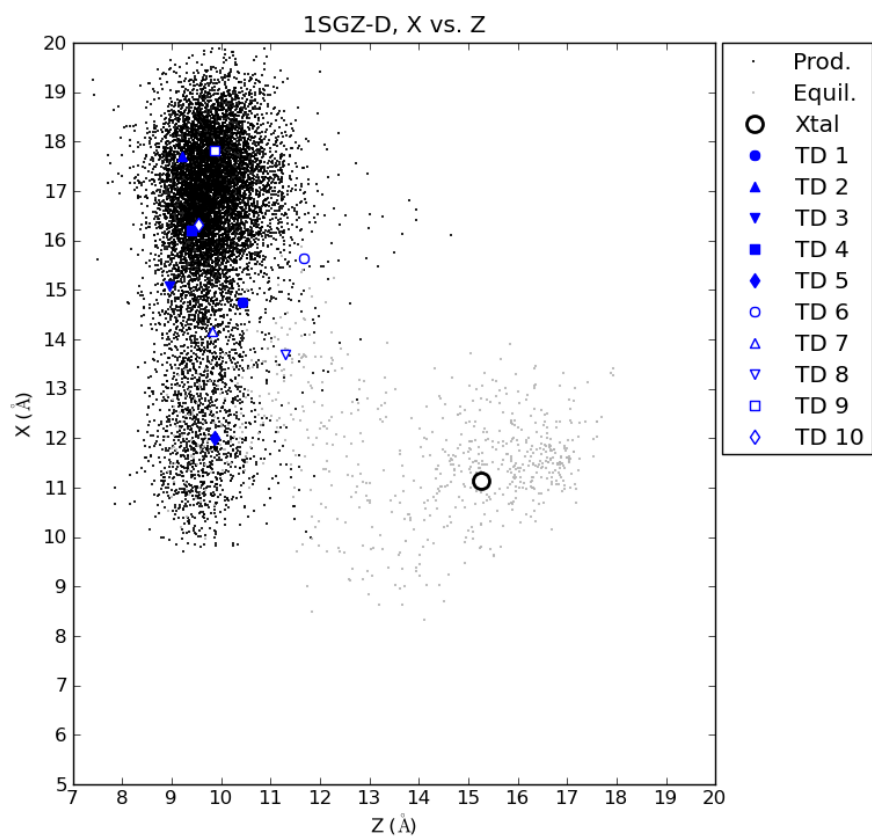


Figure S13. XZ and YZ scatter plots for simulation 1SGZ-D. Relevant centroid values are overlaid (TD: TyrDown centroid).

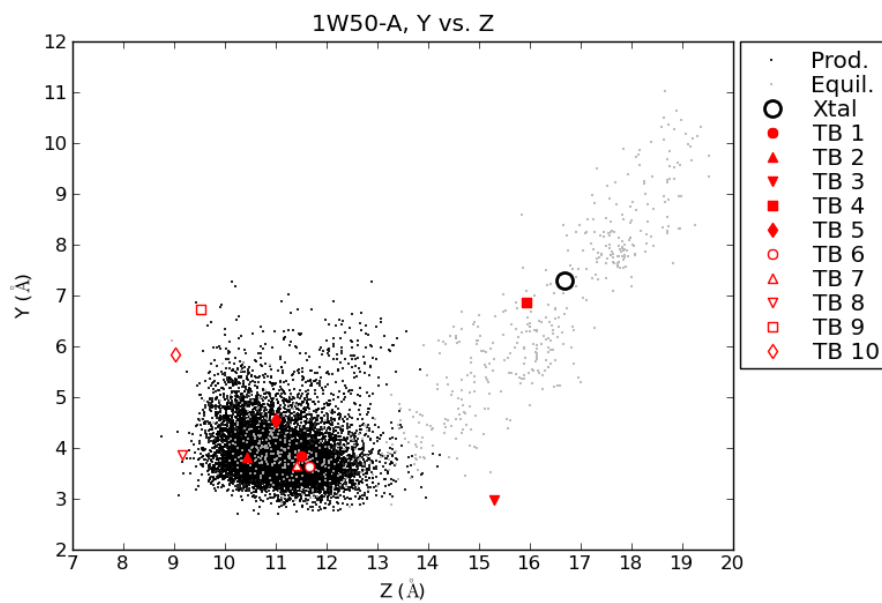
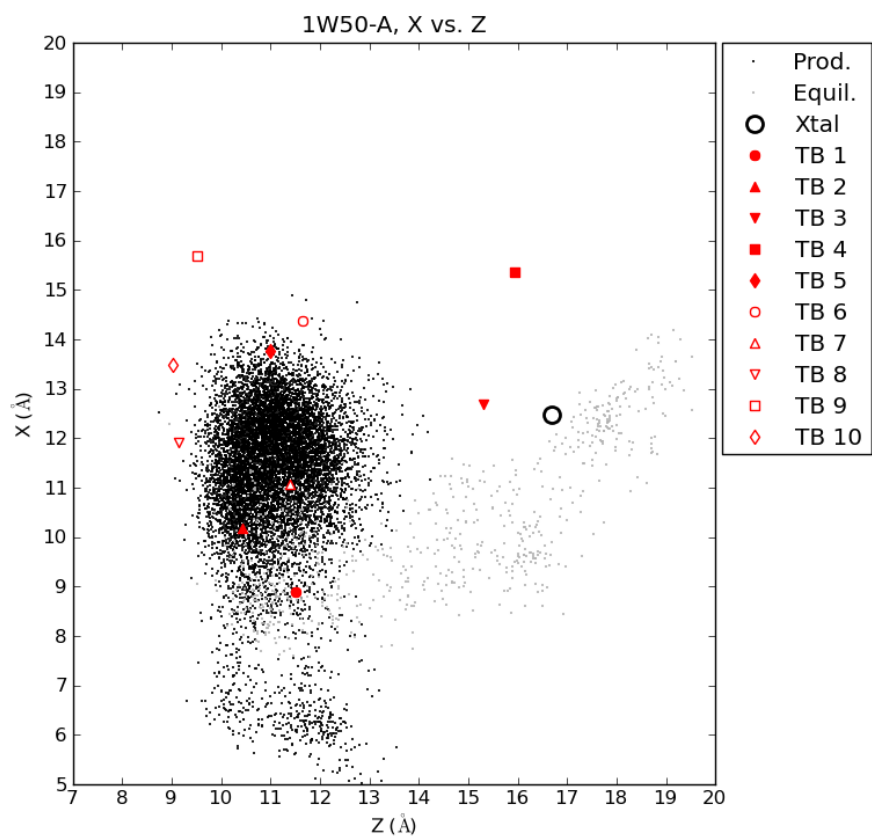


Figure S14. XZ and YZ scatter plots for simulation 1W50-A. Relevant centroid values are overlaid (TB: TyrBack centroid).

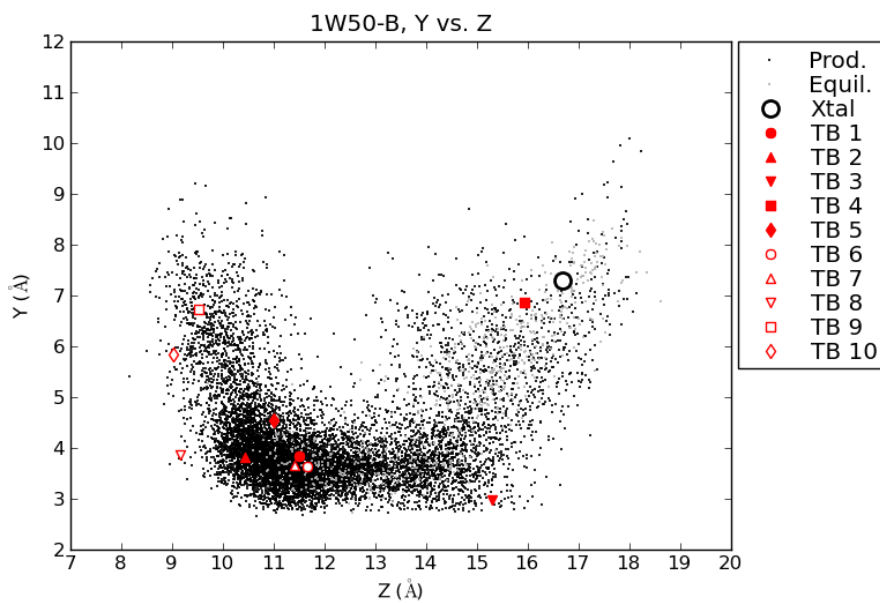
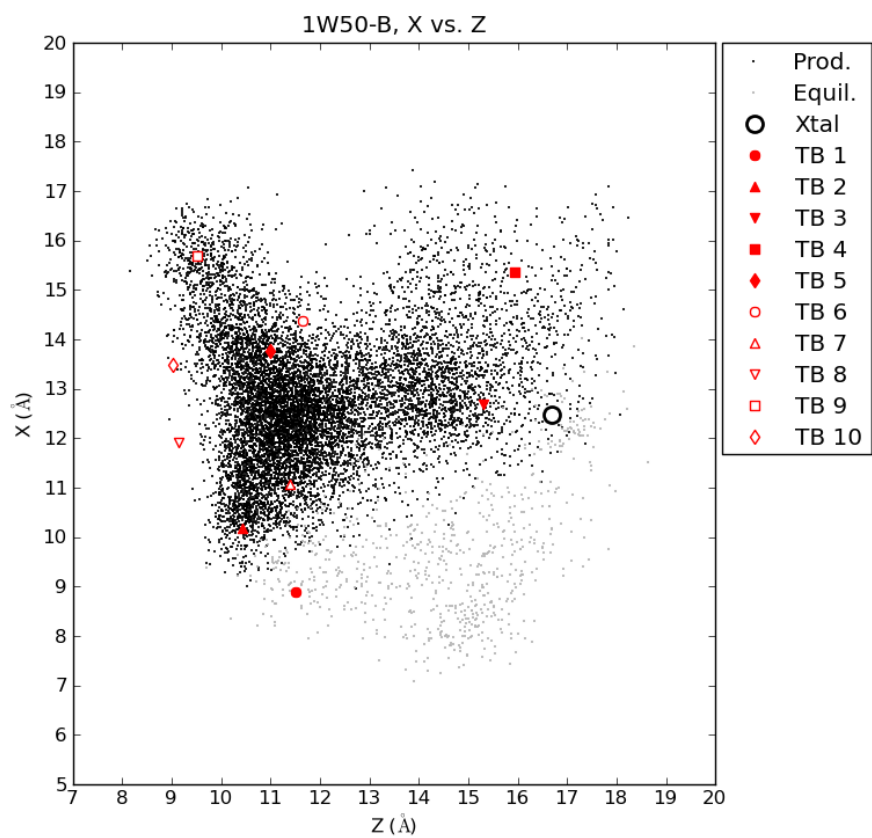


Figure S15. XZ and YZ scatter plots for simulation 1W50-B. Relevant centroid values are overlaid (TB: TyrBack centroid).

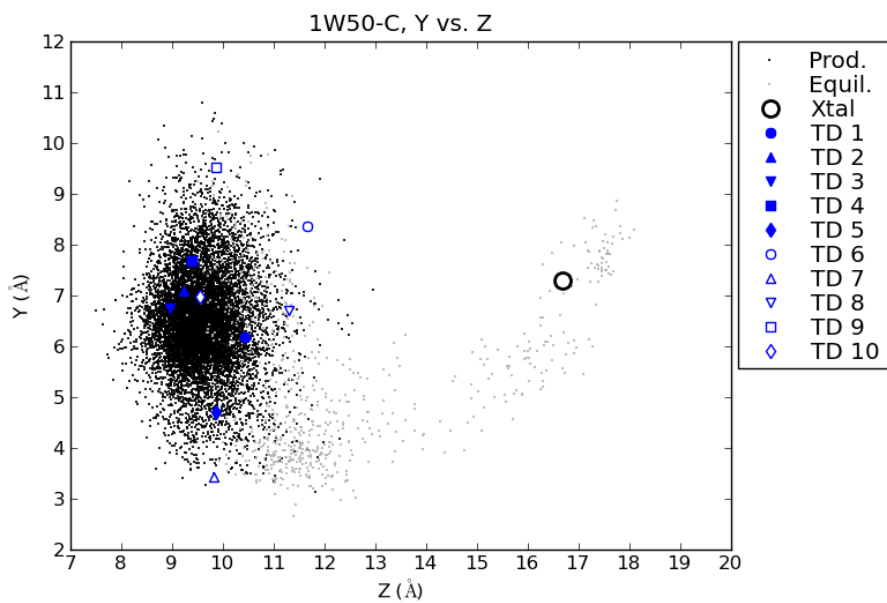
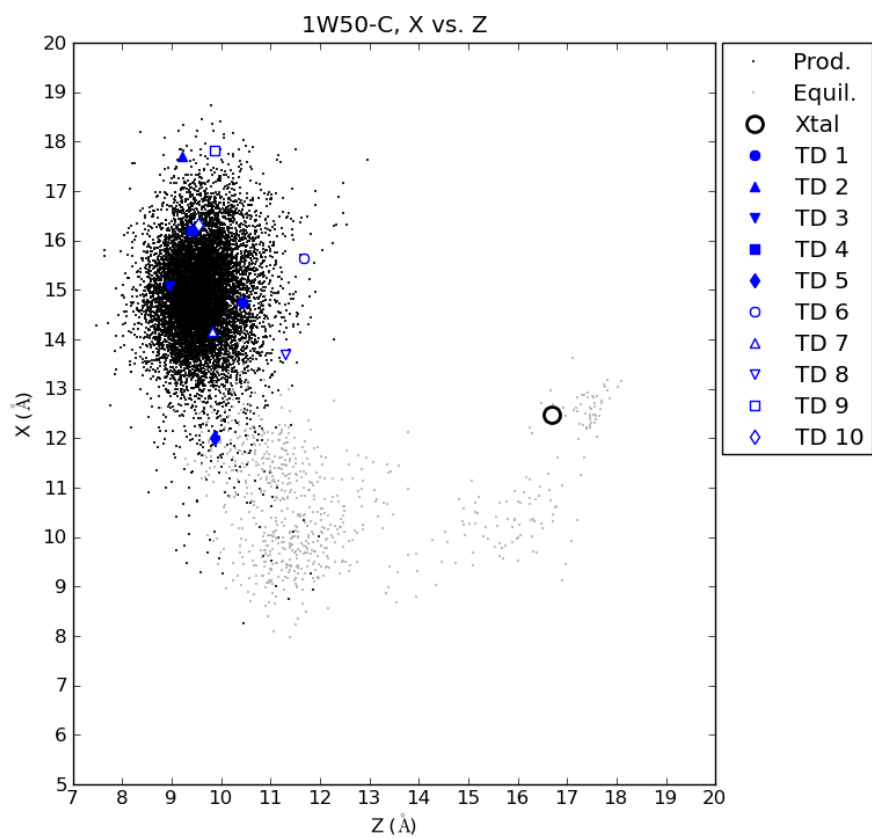


Figure S16. XZ and YZ scatter plots for simulation 1W50-C. Relevant centroid values are overlaid (TD: TyrDown centroid).

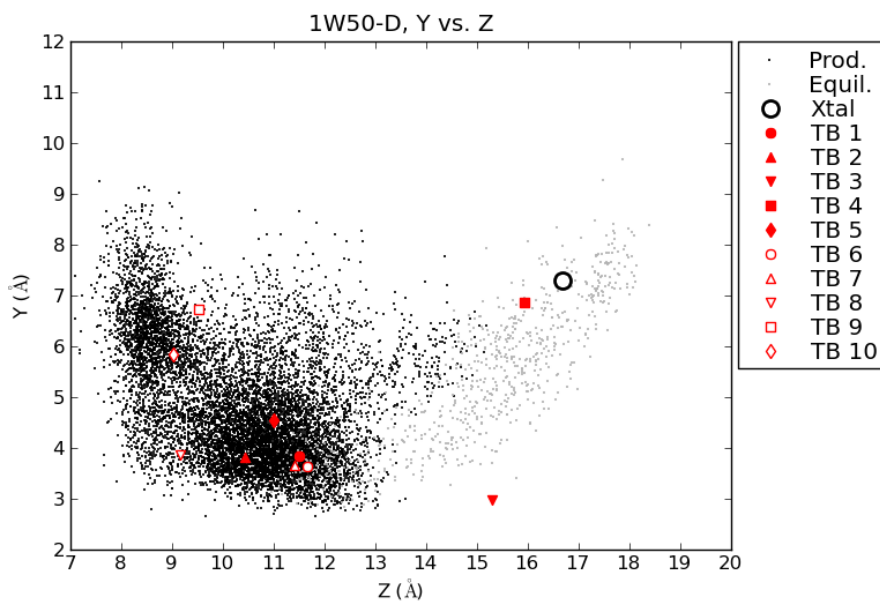
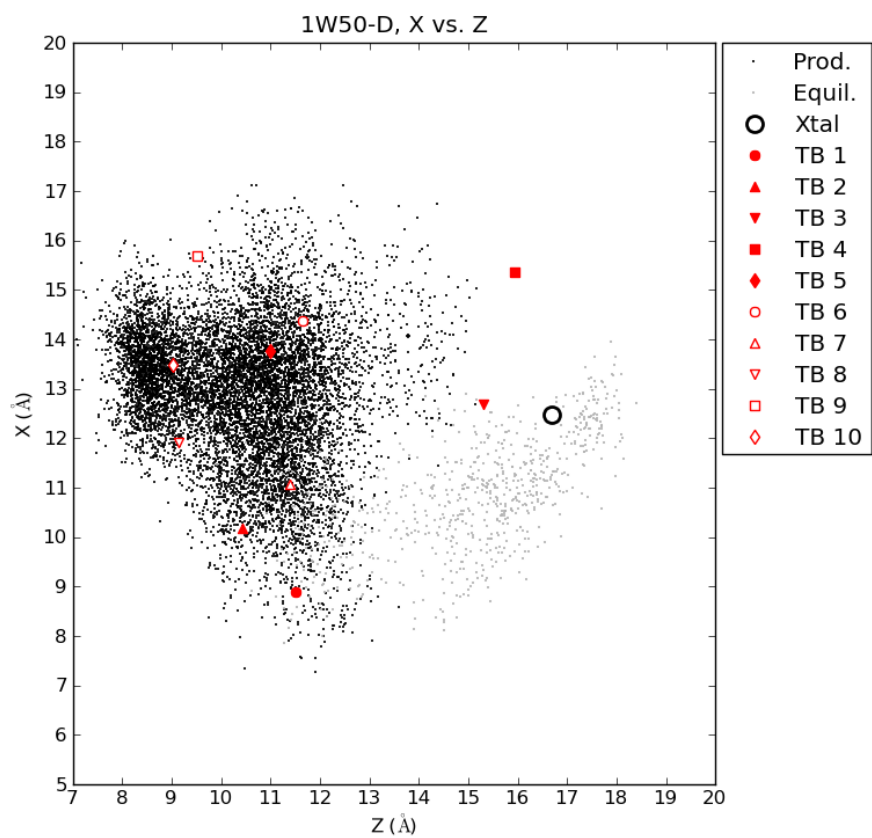


Figure S17. XZ and YZ scatter plots for simulation 1W50-D. Relevant centroid values are overlaid (TB: TyrBack centroid).

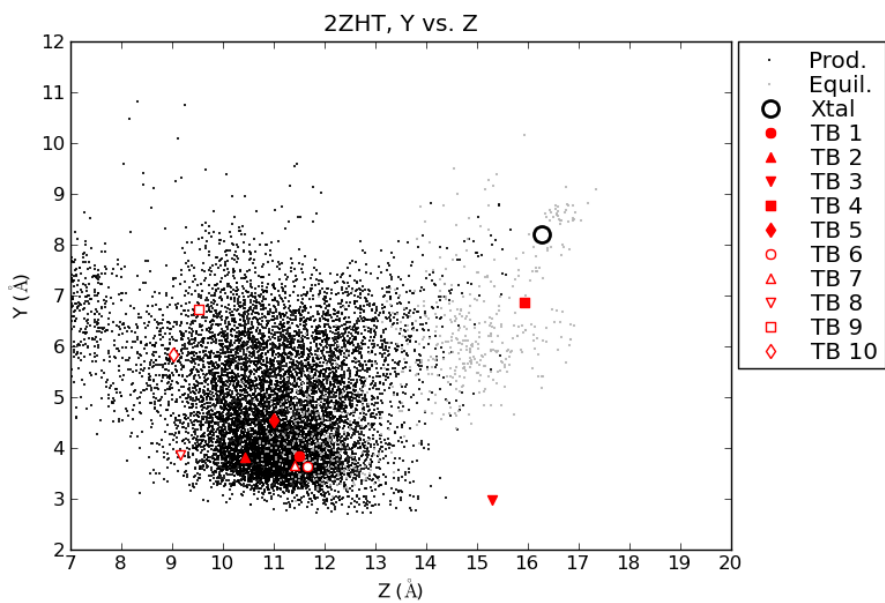
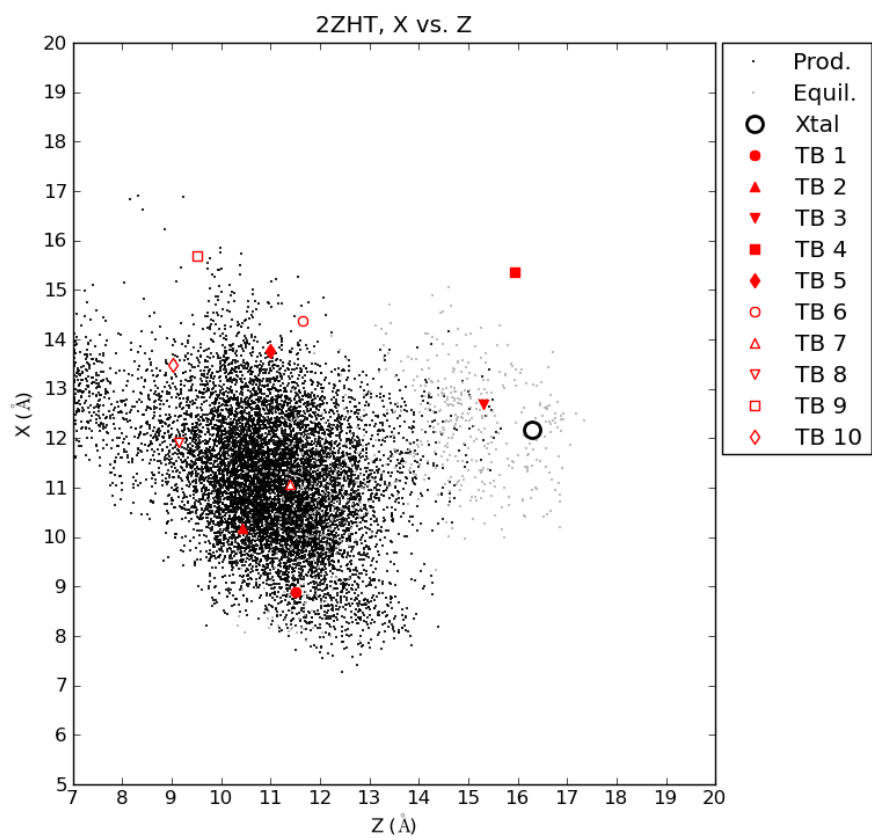


Figure S18. XZ and YZ scatter plots for simulation 2ZHT. Relevant centroid values are overlaid (TB: TyrBack centroid).

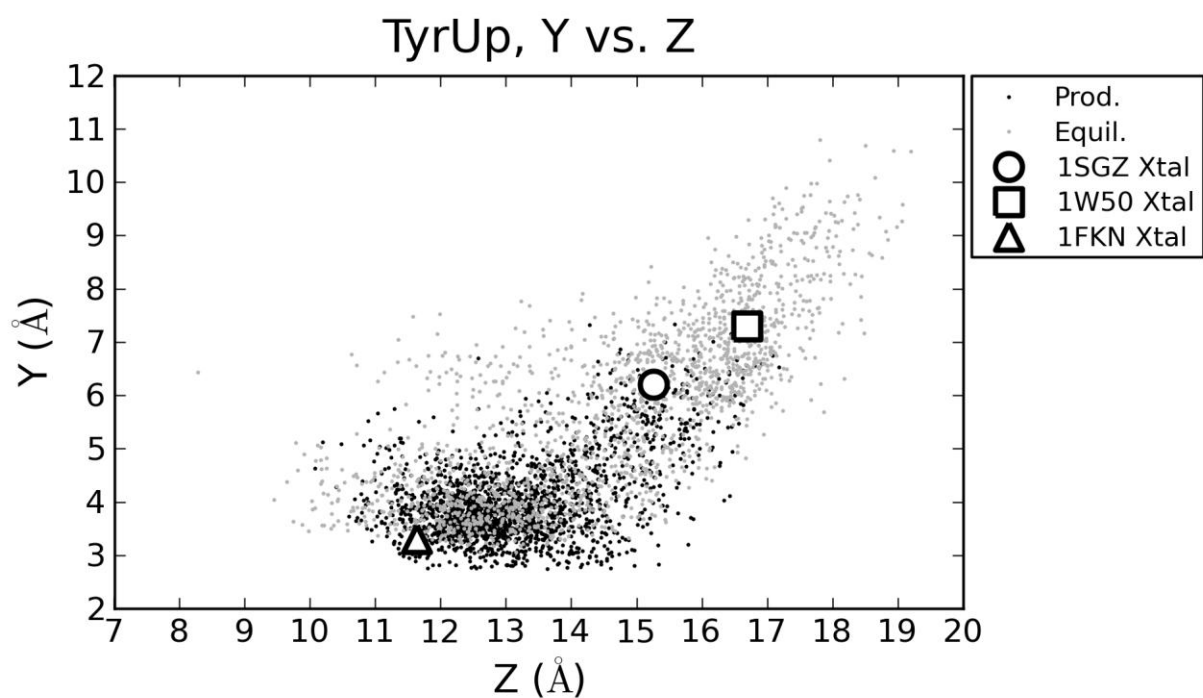
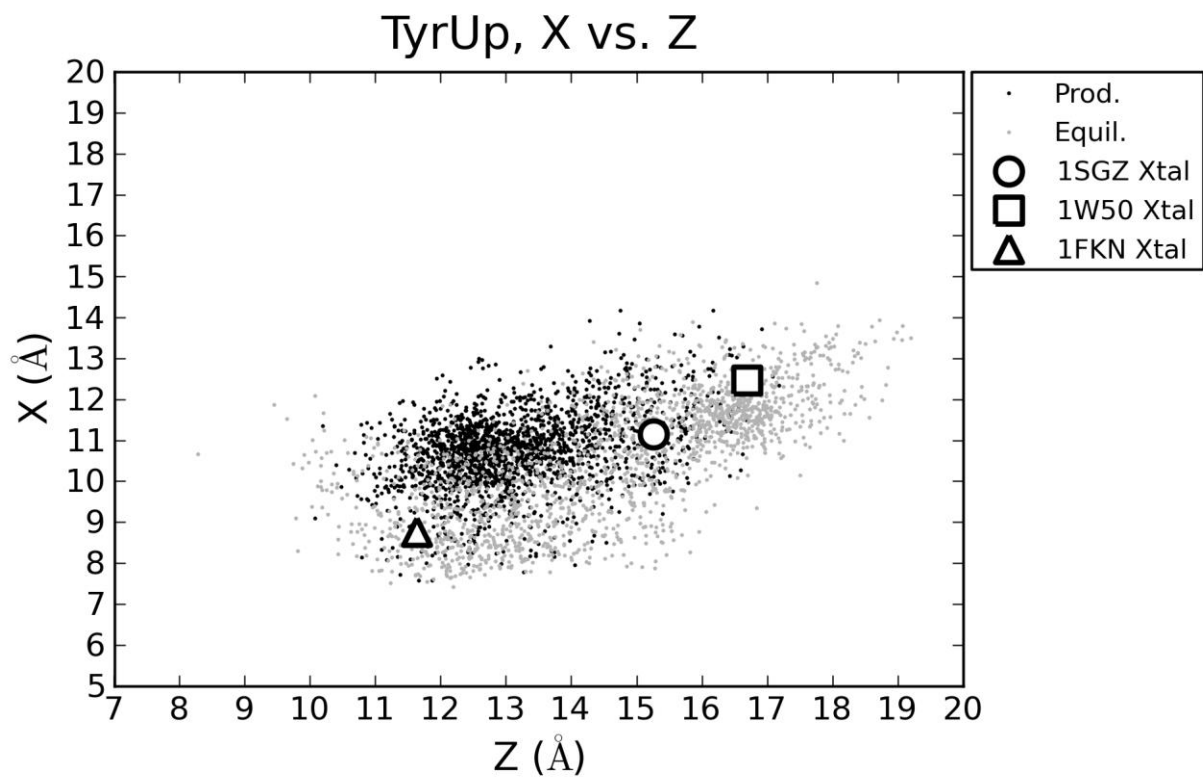


Figure S19. XZ and YZ scatter plots for all frames with Tyr71 in the TyrUp orientation. Crystal structure values are overlaid.

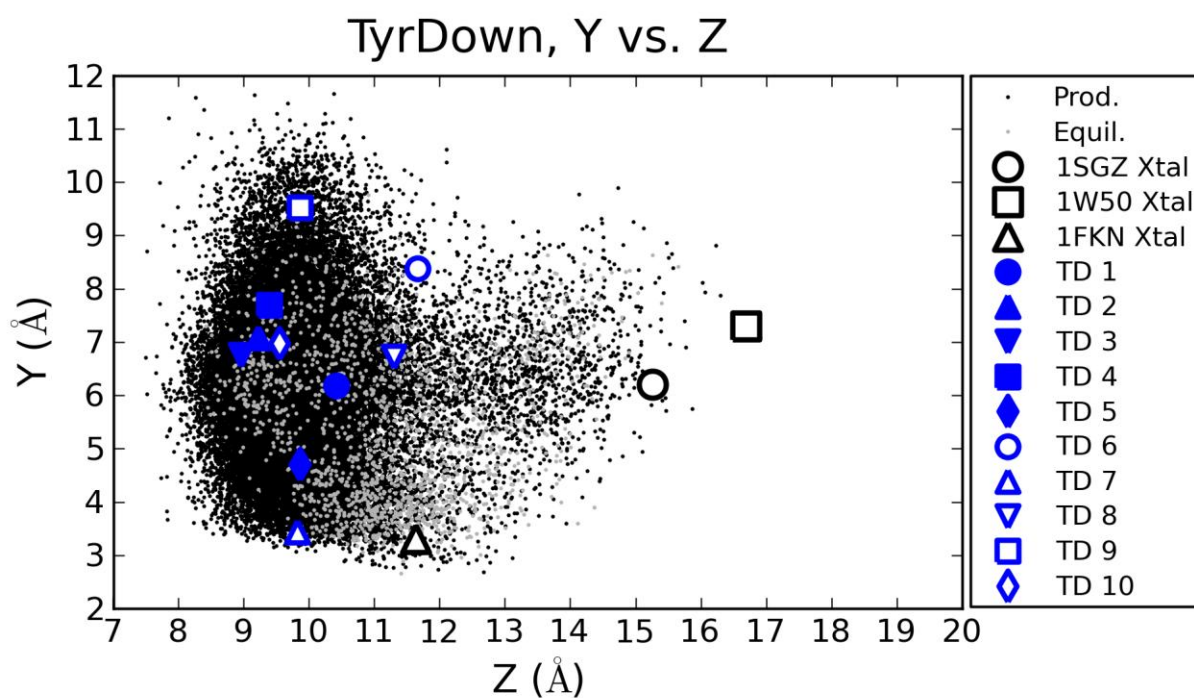
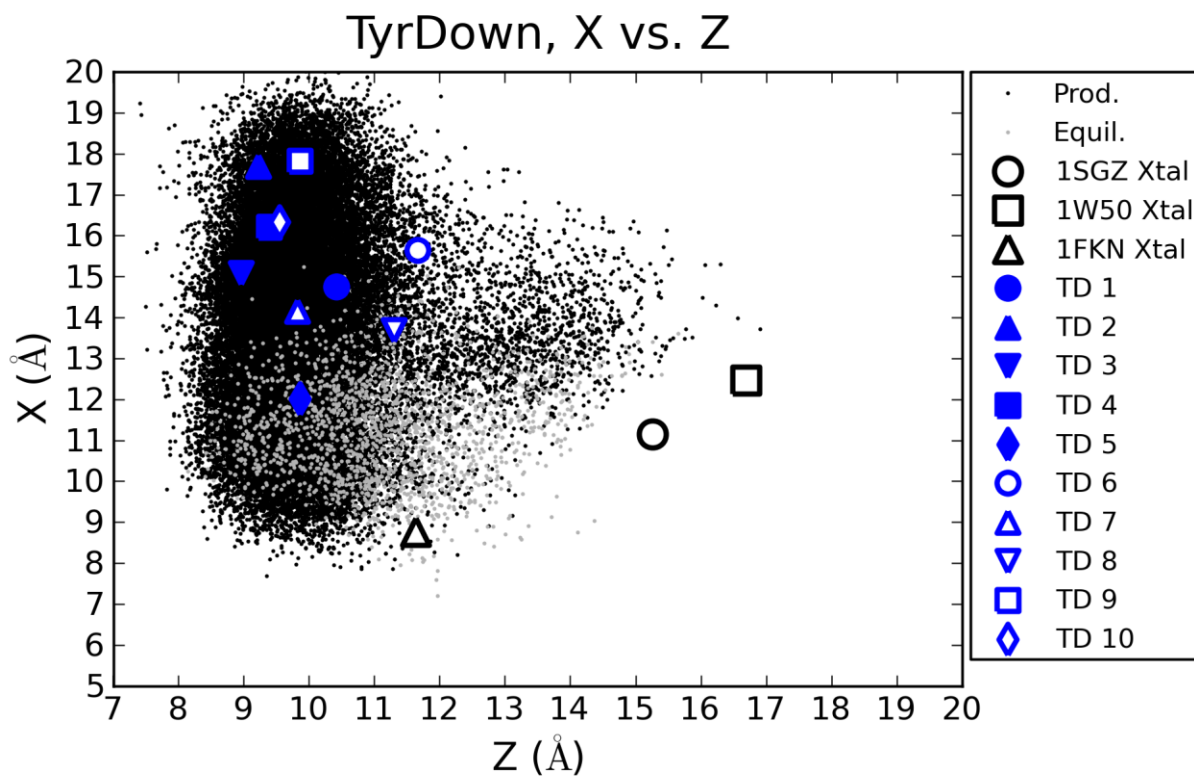


Figure S20. XZ and YZ scatter plots for all frames with Tyr71 in the TyrDown orientation. Crystal structure values and relevant centroid values are overlaid (TD: TyrDown centroid).

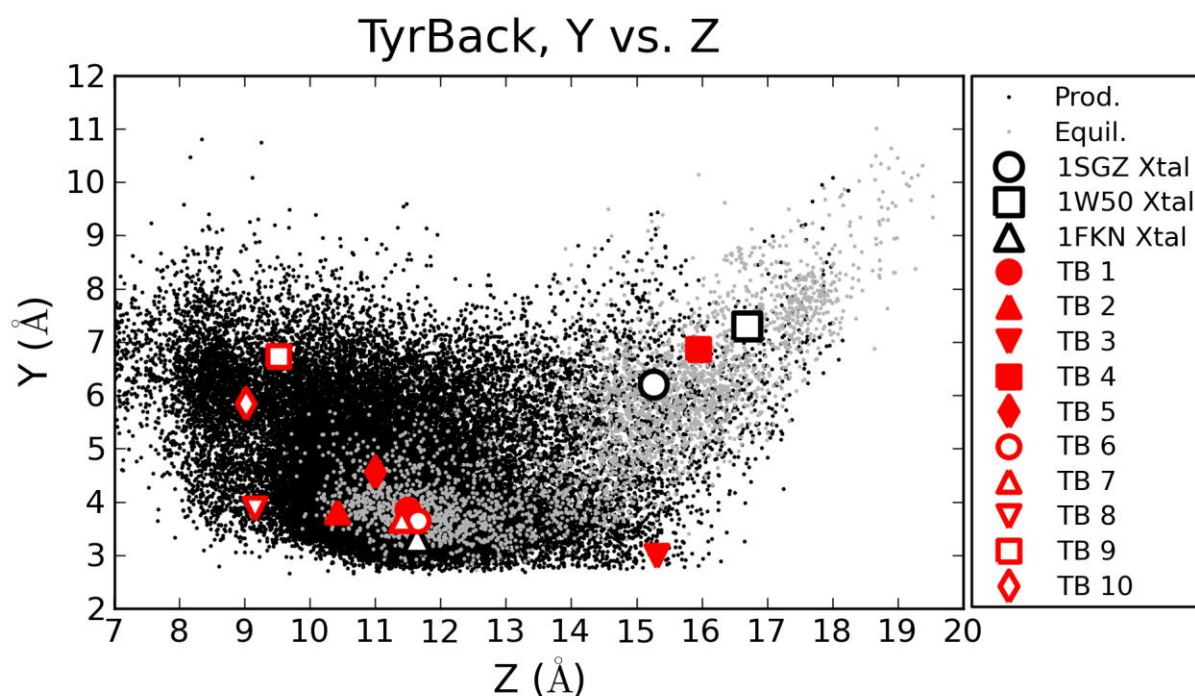
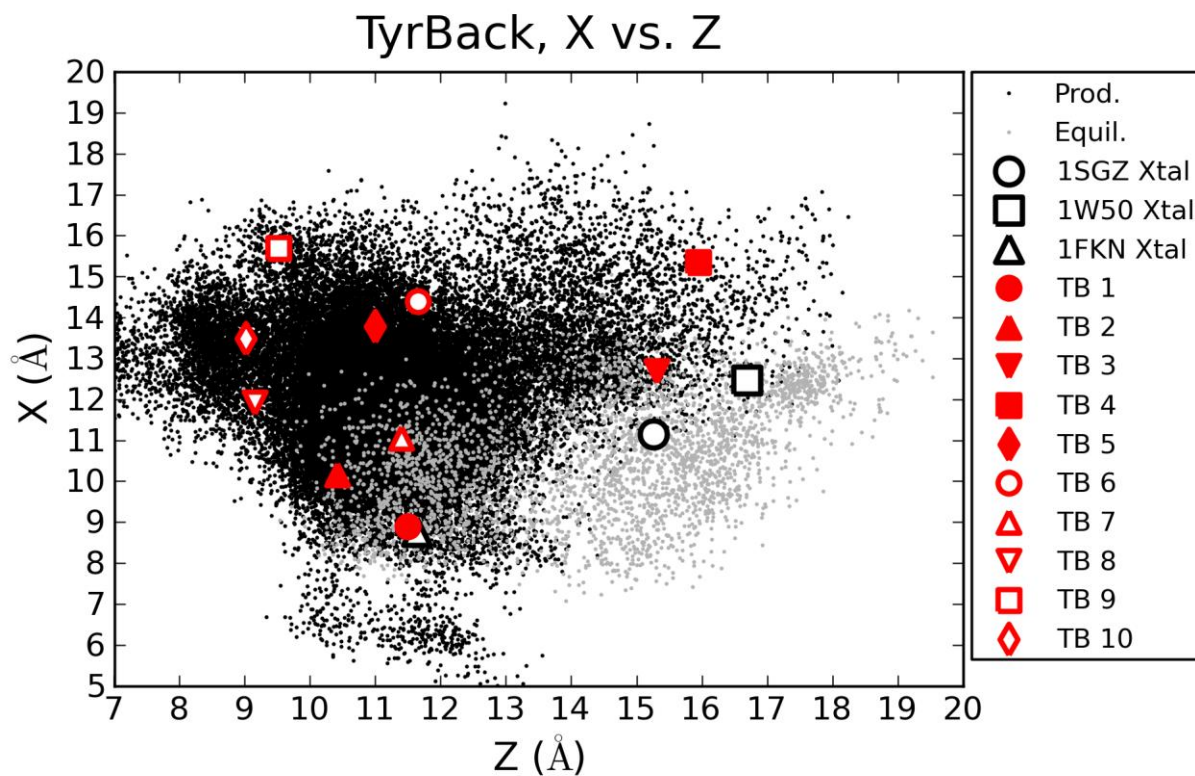


Figure S21. XZ and YZ scatter plots for all frames with Tyr71 in the TyrBack orientation. Crystal structure values and relevant centroid values are overlaid (TB: TyrBack centroid).

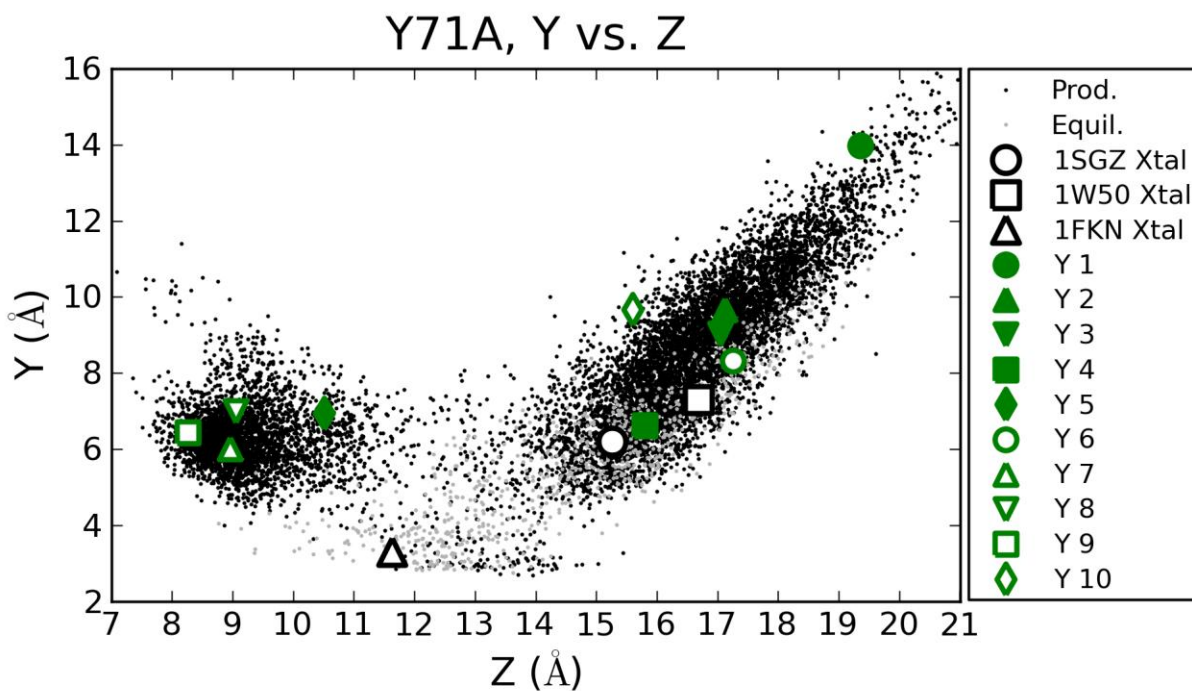
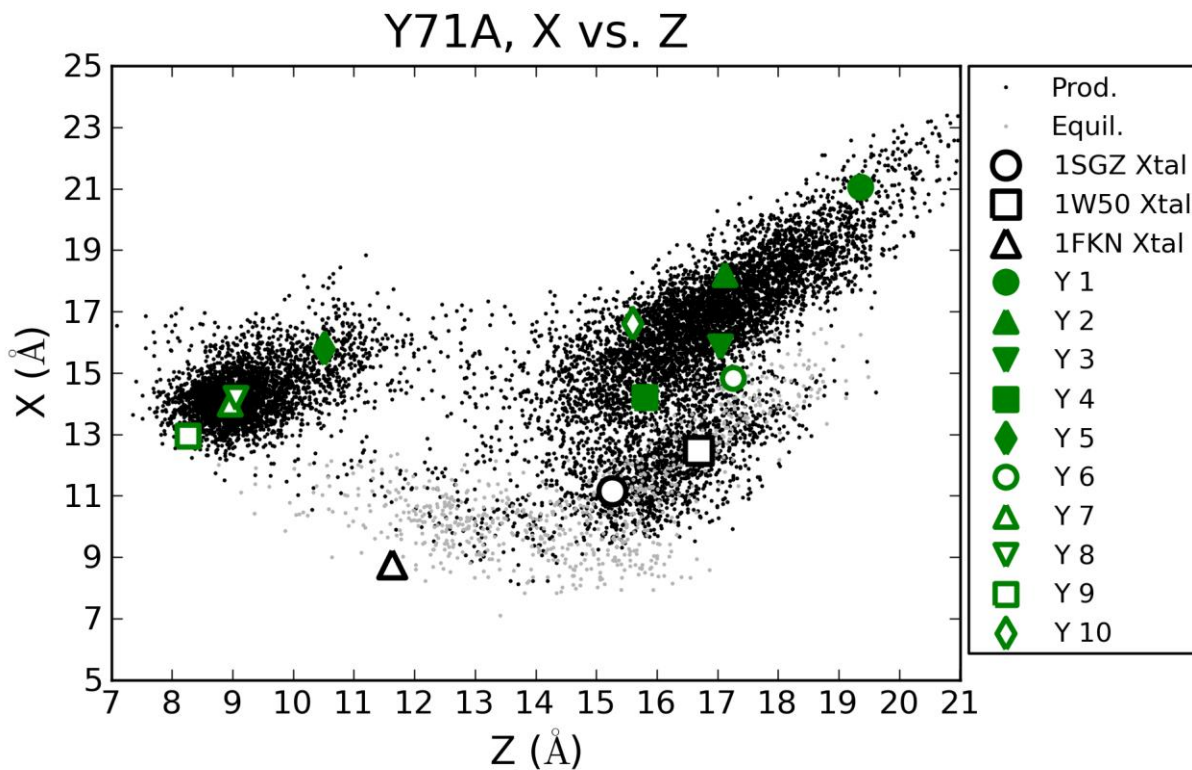


Figure S22. XZ and YZ scatter plots for all Y71A frames. Crystal structure values and relevant centroid values are overlaid (Y: Y71A centroid).

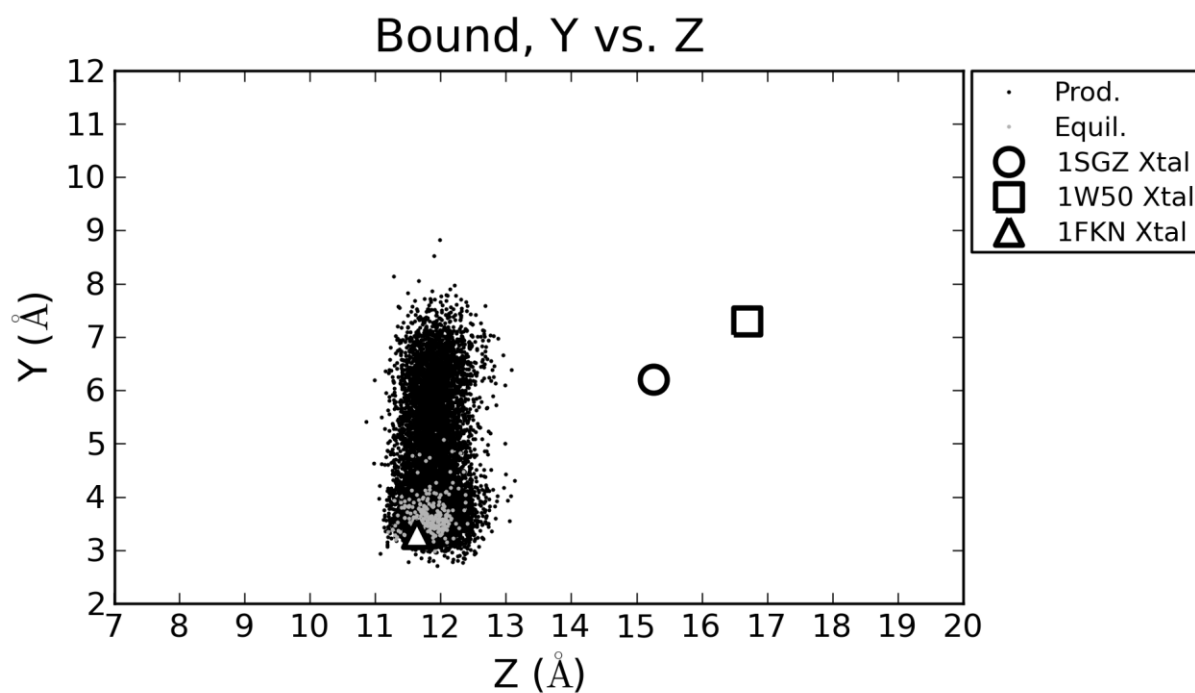
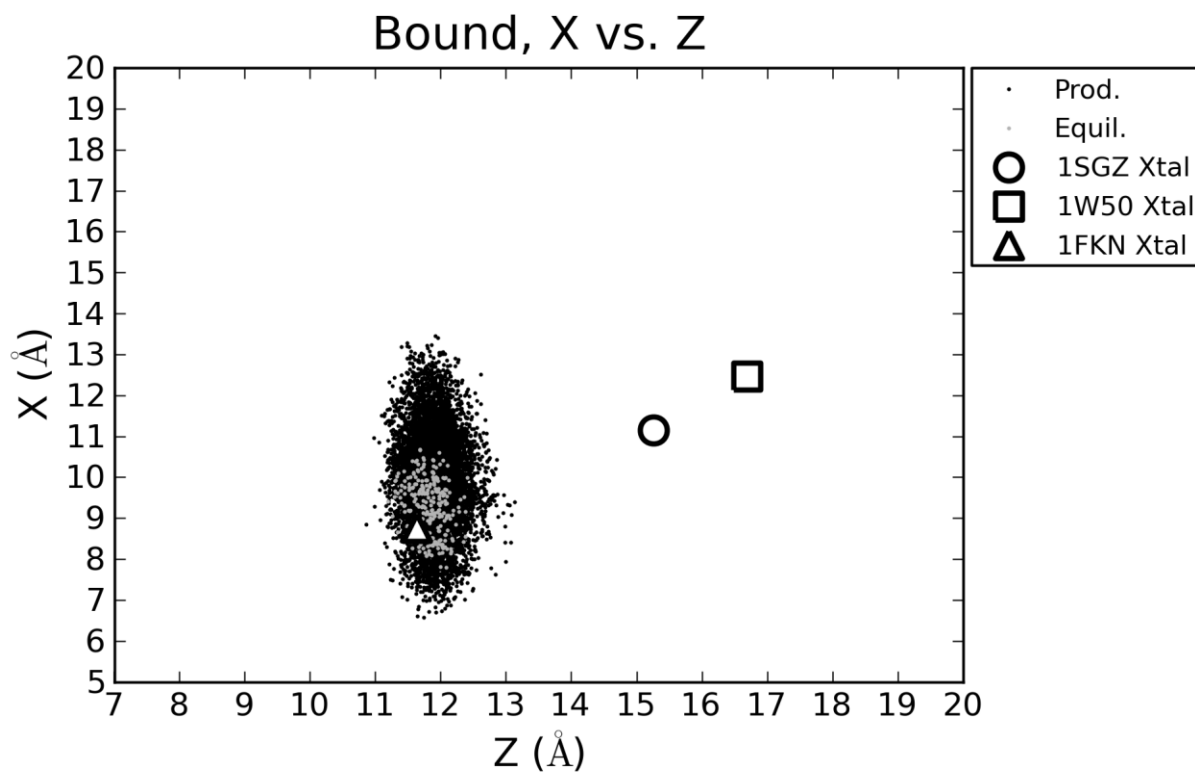


Figure S23. XZ and YZ scatter plots for all ligand-bound frames from 1FKN simulation. Crystal structure values are overlaid.

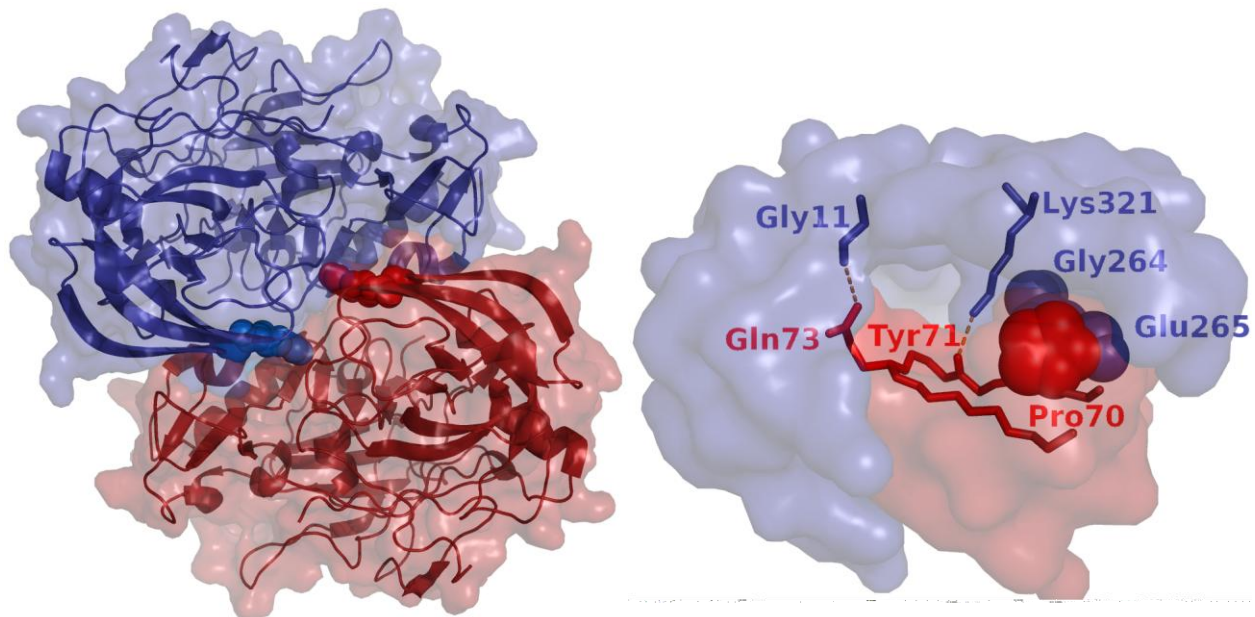


Figure S24. Crystallographic contacts in the 1W50 structure between the flap and the protein's symmetric partner. Crystal mates are shown as different colors. (Left) Zoomed out view showing the interdigitation of the flap (spheres) in the crystal. (Right) Zoomed in view of one flap and its interactions with the adjacent protein.